UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/355,210	07/12/2000	Raffaello Giorgi	515-4167	6135

7590 12/06/2001

James V Costigan
Hedman Gibson & Costigan
1185 Avenue of The Americas
New York, NY 10036-2601

EXAMINER	
LUKTON, DAVID	

ART UNIT	PAPER NUMBER
1653	16

DATE MAILED: 12/06/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/355,210	Giorgi
Examiner	**Art Unit**
David Lukton	1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on Oct 1, 2001

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-15 is/are pending in the applica

4a) Of the above, claim(s) 4 is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 1-3 and 5-15 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

Pursuant to the directives of paper No. 15 (filed 10/1/01), claims 1-3, 5-13 have been amended, and claim 15 added. Claims 1-15 are pending. Claims 10-14, previously withdrawn, are now rejoined with the elected group. Claim 4 remains withdrawn from consideration; claims 1-3, 5-15 are examined in this Office action.

*

Applicants are reminded of the preferred arrangement of the specification:

(a) Title of the Invention.
(b) Cross-References to Related Applications.
(c) Statement Regarding Federally Sponsored Research or Development.
(d) Reference to a "Microfiche Appendix" (see 37 CFR 1.96).
(e) Background of the Invention.
    1. Field of the Invention.
    2. Description of the Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(f) Brief Summary of the Invention.
(g) Brief Description of the Several Views of the Drawing(s).
(h) Detailed Description of the Invention.
(i) Claim or Claims (commencing on a separate sheet).
(j) Abstract of the Disclosure (commencing on a separate sheet).
(k) Drawings.
(l) Sequence Listing (see 37 CFR 1.821-1.825).

It is suggested that the section entitled "state of the art" (page 3) be moved to the beginning of the first page.

- In addition to the foregoing, the specification (p. 6, line 13) makes reference to an "attached diagram". To what does this refer? If this refers to the reaction scheme on page 29, this should be made clear.

- Deletion of the reaction scheme on page 29 is required. As stated in 37 CFR 1.58:

  "The specification, including the claims, may contain chemical and mathematical formulas, but shall not contain drawings or flow diagrams"

  Submission of formal drawings is required, accompanied by deletion of the reaction scheme from page 29. The formal drawings must conform to 37 CFR 1.81. In addition, a figure legend is required.

- An abstract is still required. An abstract has been submitted in which one piece of paper is taped onto another. However, this is not permitted. Resubmission of an abstract on one piece of paper is required.

*

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 5-15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In the specification as filed, there was a requirement that when R_1 and R_2 represented benzyl, neither of R_3 and R_4 could represent isopropyl. This proviso has now been deleted. The compounds now encompassed were not described in the specification as

filed; accordingly, new matter has been introduced.

*

Claims 8-9 and 14 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants have asserted (p. 27) that they have subjected "the compounds of the invention" to *in vitro* assays, as described on page 27 (and references cited therein). Applicants have also asserted that "the compounds of the invention" were "active" in the assays. These assertions are left unchallenged at this time. To take it a step further, the examiner will stipulate that claims 11-13 are enabled. In claims 8-9, applicants assert that the compounds are effective to treat various diseases. However, there is no evidence that this is the case. Merely because the asserted antagonism may take place *in vivo* does not mean that there exists a single disease or disorder for which benefit will accrue to a patient. The degree of antagonism might not be sufficient to achieve a perceptable effect; moreover, the NK-2 receptor might not be a critical element in any of the recited disorders, i.e., even if the NK-2 receptor could be blocked to the extent of 100% *in vivo*, it does not necessarily mean that the symptoms of any disease will recede.

Even the expenditure of "undue experimentation" may not be sufficient to enable one to treat the cited diseases.

*

Claims 1-3, 5-15 are rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- In claim 1, line 1, the term "general" is superfluous.
- In claim 2, line 1, the term "compounds" should be in the singular.
- In claim 2, third line from last, the following is recited:

  "-R5, R6, R7 are H["

  What is the significance of the left-handed bracket?

- In claim 3, at least 6 of the compound names are followed by a period; this period is followed by the designation "TFA". However, all of the periods in claim 3 should be eliminated, except for the one at the very end of the claim. In addition, if the designation "TFA" is going to be used, it must be accompanied by the definition of the term which this abbreviation represents.
- In claim 5, the term "excipients" should be in the singular.
- In each of claims 6 and 7, the term "antagonists" should be in the singular.
- Claim 9 is not enabled. Setting that aside, however, the term "anxiolytics" should be in the singular.
- Each of claims 7 and 11-13 recites the abbreviation "NK-2". This term may be used, but only if accompanied by the fully name of the term that this abbreviation represents (presumably neurokinin-2).
- Claim 10 is drawn to a method of antagonizing tachykinin. How is this possible, biochemically? That is, how is it possible to antagonize tachykinin, while leaving the tachykinin receptors unaffected? Is there an assay which applicants are aware of, or which can be hypothesized, which could demonstrate

this? It is suggested that the claim be limited to antagonizing the receptor only.

- Claim 10 recites "tachykinin peptide receptors". It appears that the term "peptide" within this phrase is superfluous.

- Claims 11-13 were amended in conformance with a previous suggestion. However, upon reconsideration, while the "contacting" of the compound with the receptor would be appropriate in claim 100 (below), it is not suitable in the case of administration to a mammal. Accordingly, claims 100-102 are suggested (applicants may insert into claim 102 the various disorders for which descriptive support exists):

  100. A method of antagonizing a neurokinin-2 (NK-2) receptor comprising contacting an NK-2 receptor with a compound according to claim 1 for a time and under conditions effective to antagonize said NK-2 receptor.

  101 A method of antagonizing a neurokinin-2 (NK-2) receptor comprising administering to a mammal in need thereof a compound according to claim 1 for a time and under conditions effective to antagonize the NK-2 receptor.

  102. The method according to claim 101 wherein said mammal is afflicted with {one of the disorders recited in claimed 8}

- Claim 14 is not enabled. However, setting that aside, the claim is indefinite as to the process steps and endpoint. It is suggested that the claim be amended to recite that the compound is administered to the patient *for a time and under conditions effective to antagonize the NK-2 receptor.*

- Claim 14 should begin with the indefinite article ("a").

- Claim 14 is indefinite as to which "products" are intended.

*

The following is a quotation of the appropriate paragraphs of 35 U.S.C §102 that form the basis for the rejections under this section made in this action.

A person shall be entitled to a patent unless -

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2 are rejected under 35 U.S.C. §102(b) as being anticipated by Rothe, M. (*Pept., Proc. Eur. Pept. Symp.* 14th, 71-8, 1976).

Rothe discloses (table 1, page 72) the compound fungisporin, which is

cyclo-Phe-Phe-Val-Val

Claim 1 is anticipated for the case of variables R_1 and R_2 representing benzyl, and R_3 and R_4 representing the side chain of valine.

*

Claims 1-2 are rejected under 35 U.S.C. §103 as being unpatentable over Kitakabake (*Peptide Chemistry*, **17**, 7, 1980).

As indicated previously, Kitakabake discloses the following compound:

cyclo-Val-Val-Phe-Phe.

The previous proviso has been eliminated; accordingly the claims are now anticipated.

*

The following is a quotation of 35 USC §103 which forms the basis for all obviousness rejections set forth in the Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claims 1, 2, 5-9, 15 are rejected under 35 U.S.C. §103 as being unpatentable over Kitakabake (*Peptide Chemistry*, **17**, 7, 1980).

The §102 rejection of claims 1-2 still applies. However, in the event that applicants re-instate the previous exclusion, claims 1-2 will then be rejected under §103 (only).

As indicated previously, Kitakabake discloses the following compound:

cyclo-Val-Val-Phe-Phe.

The reference does not disclose any of the following:

cyclo-Leu-Val-Phe-Phe.

cyclo-Val-Leu-Phe-Phe.

cyclo-Ile-Val-Phe-Phe.

cyclo-Val-Ile-Phe-Phe

Applicants have argued that the reference provides no motivation to modify the structure of the cyclopeptides. However, the question is not whether the peptide biochemist of ordinary skill would have expected better "gushing" effect in beer, but rather, whether the the peptide biochemist of ordinary skill would have expected substantially the same "gushing" effect in beer. The assertion is that the peptide biochemist of ordinary skill would have expected substantially the same gushing effect. Note that, in order for this rejection to be valid, there is not need to ascribe to the biochemist of ordinary skill any opinion one way or another about the effect of any peptide on NK-2 receptors.

As for the composition claims, merely placing the peptide in aqueous solution generates a composition. As for claim 15, the reference teaches more than one stereoisomer.

The rejection is maintained.

✺

It is suggested that applicants amend claim 4 as deemed appropriate. Currently, the following is present in claim 4:

"[compounds] are made to react as shown in the diagram".

This phrase will have to be deleted, and replaced with something more specific. In addition, claim 4 should recite a step for isolation of the final product.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton. Phone: (703) 308-3213.

An inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

DAVID LUKTON
PATENT EXAMINER
GROUP 1800